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SYSTEMIC BLASTOMYCOSIS.

(FINAL REPORT OF THE CASE DESCRIBED BY EISENDRATH AND ORMSBY IN 1905.)

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In this article we wish to describe the termination and the results of the anatomical study of the case of systemic blastomycosis reported by Eisendrath and Ormsby[1] in 1905. As stated in their report, the patient was a Polish laborer, age thirty-three, married, and the father of two children. The illness began in February, 1904. The following version of the beginning is given by them:

> The first noticeable departure from his usual good health consisted in a feeling of discomfort involving the chest on the right side, extending through from front to back. This lasted for a time, being better and worse at intervals. In June his first cutaneous lesion appeared. This was located below the left ankle and extended down to the heel, and eventually became a little larger than a dollar. Shortly afterward the other lesions appeared, but it was impossible to tell their exact mode of development. In addition to the area on the left leg, the right leg had several large lesions, also the right and left forearm, and the face, chin, and neck, especially on the right side. About November, 1904, he suffered great muscular weakness, and marked swelling of the feet and ankles occurred. This gradually increased until he was wholly unable to work. He stopped work in December. . . . . On his admission to the hospital in February, 1905, he presented lesions on all the above-mentioned areas, and was very much emaciated, pale, anemic, exceedingly weak, and had some elevation of temperature. Marked edema was present in the ankles, feet, face, and arms. His nails were clubbed, and moderate inguinal adenopathy was noted. . . . . All the lesions were quite superficial, the larger part of each being an ulcer, crust-covered in places, open in others. There was little induration, but considerable sanguinopurulent discharge. The edge of the ulcer was slightly elevated and presented a bluish-red halo, in which there were located a few miliary abscesses. In some parts of the area a papillomatous condition was present. The lesion on the arm was a subcutaneous nodule, which later softened and was incised, and from the sinus left after this procedure, and from both the lesions on the legs, the organism of blastomycosis was demonstrated.
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> On April 26 blastomycetes were demonstrated in the blood-stained muco-purulent sputum. Tubercle bacilli were not found either in the sputum or in the pus, and there was no reaction to tuberculin. Liver and spleen not palpable May 1. Right apex and upper right lobe dull posteriorly with bronchophony and bronchial breathing. A few râles in right lower lobe. During his four-months' sojourn in the hospital the

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[1] *Ill. Med. Jour.*, 1905, 8, p. 454; *Jour. Am. Med. Assoc.*, 1905, 45, p. 1045.

temperature ranged from 98.6° to 102.8°. On July 7, when the patient left the hospital, he was much improved in every way. Five weeks later he suffered a relapse with marked pain in the right chest, several cutaneous lesions were again active, and the sinuses leading from the deep lesions on the forearm had reopened. Eisendrath and Ormsby also report the following cultural and animal experiments:

"The first cultures on March 8 were made from open ulcers and a sinus on the forearm, and although the organism was fairly abundant in smears made from the pus, it failed to grow on the media. On March 22 pus was removed from a subcutaneous abscess on the left forearm, which was inoculated on various media. Six days later growth was plainly visible, and after this time the cultures grew rapidly. These proved to be pure cultures of blastomycetes. . . . . In the pus they occurred as circular and budding forms, having a double contour and the usual refractile capsule. On media the growth varied. It presented a moist, pasty surface on glycerin-agar, with at times a wormy appearance, or else presenting large folds and depressions. Microscopically, these cultures showed many oval and circular organisms, some budding ones, and much mycelial formation, the latter being both coarse and fine and containing sporules. Lateral conidia occurred. On glucose-agar the growth was more dry, white, and presented aerial hyphae; and microscopically there were fewer circular and budding organisms and more fine mycelia. On both glucose and glycerin-agar the media were penetrated to a considerable depth in a semicircular manner. On blood serum the growth was also moist and pasty, and presented a greater proportion of the circular and oval organisms. The cultures taken from the cutaneous lesions, the subcutaneous abscesses, and the sputum all appeared similar. Subcultures had to be made to obtain pure cultures from the sputum. On April 26 two guinea-pigs were inoculated subcutaneously with an emulsion of pus and granulation tissue, removed from the forearm by incision into an unruptured, deep-seated abscess. Both these animals developed a local lesion of blastomycotic infection at the point of inoculation and surrounded it for half an inch in each direction. These lesions remained for a few weeks, then healed, leaving only a slight atrophic area."

Tuberculosis did not develop in any of four guinea-pigs inoculated with pus, sputum, or granulation tissue.

After leaving, as stated by Eisendrath and Ormsby, on July 27, 1905, he returned two months later to the service of Dr. Eisendrath. A gibbus opposite the fourth dorsal vertebra was observed at this time and motion was impaired; the trunk and extremities showed pustular lesions. Sinuses in the forearm and legs were curetted; one of these communicated with the ankle joint of the left side, and denuded bone was demonstrated.

On November 21 he was transferred to the medical service, at first of Dr. Goodkind, subsequently of Drs. Herrick and Wells. His appearance then was that of a fairly well-nourished man who was not very ill. On the arms and feet elevated ulcers were present covered with crusts, also healed ulcers with loose cicatrices. Active ulcers were also present in the right subscapular region; the posterior cervical glands were palpable. The respiratory motion was noticeably lessened on the right side, and tactile fremitus was increased over the right lung behind and laterally, where impaired resonance bronchial and broncho-vesicular breathing, and numerous moist and whistling râles were obtained. Early in March, 1906, pus began to escape from the gibbus; there are no records of its examination. The hepatic dulness is noted as reaching nearly to the umbilicus in June; new lesions appeared on the face in July, and there were alternate periods of diarrhea and constipation throughout his illness, except toward the end when diarrhea became pronounced. The feces were examined at this time and found to contain considerable quantities of blood and muco-purulent exudate. Dr. Fischmann, who examined them, also reported finding blastomycetes repeatedly with budding forms. Blood also appeared at times in the urine with albumin and casts; a few days before death the urine contained no albumin, but microscopic examination revealed red blood cells and a few casts. Several examinations of the blood were made; a slight leucocytosis was generally found, the different varieties of leucocytes maintaining normal proportions; at no time was an eosinophilia present.

Both knees became ankylosed in a partially flexed position; they, as well as the left elbow joint, were enlarged and tender, but showed no local increase in temperature or redness; extension was difficult and knee reflexes could not be tested. The cutaneous sensibility was not examined. He frequently voided urine with no knowledge of the fact, and during the last four months of his life the bowel movements were also involuntary. The left arm and both legs became edematous; the sinuses mentioned persisted, and on pressure a thick brownish pus of peculiar odor escaped from them. Over both trochanters large decubital necroses developed and a slight general adenopathy. Death occurred during a convulsion on August 23, 1906.

During these months in the hospital an evening rise of temperature usually occurred; the highest was 102.8°. Blastomycetes were repeatedly found in the sputum, and persistent efforts to demonstrate tubercle bacilli gave negative results.

The body was examined a few hours after death and the following anatomical diagnosis made: Blastomycotic bronchopneumonia; blastomycosis of the peribronchial lymph nodes, of the pleura, the subpleural, and retropharyngeal tissue, the liver, the kidneys, the colon, the spinal column (dorsal vertebrae), the external spinal dura, the cerebellum, the left elbow, both knee and ankle joints, and of the skin and subcutaneous tissue with ulcerations, fistulae, and scars. Fibrous induration at root of right lung. Fibrous pleuritis. Passive hyperemia of liver and spleen. Serous atrophy of adipose tissue. Emaciation. Adenoma of thyroid and accessory spleen.

The following are some of the more interesting details: "The body, still warm, is 167 cm. long and much emaciated. There is an abscess over the right parietal bone, edema of both eyelids, a smooth, loose scar on the lower part of the face involving the lower lip; the volar surface of the right forearm has three sinuses leading into as many abscesses, all exuding pus on pressure; pressure on the left elbow, which is twice the normal size, causes flow of pus from several openings in the forearm; this joint and both ankle joints crepitate and fluctuate. About the ankle joints are similar sinuses. There are scars on the legs, and between the shoulders is a large, reddened, edematous, and pigmented region from which many sinuses open; there is a gibbus at the level of the fourth dorsal vertebra.

"The abdominal wall is thin, the muscles pale and atrophied, the peritoneum smooth, the lower margin of the liver 8 cm. below the costal margin in the median line. There are no adhesions in the cavity and only a small amount of fluid. The mesenteric adipose tissue is gelatinous in consistency.

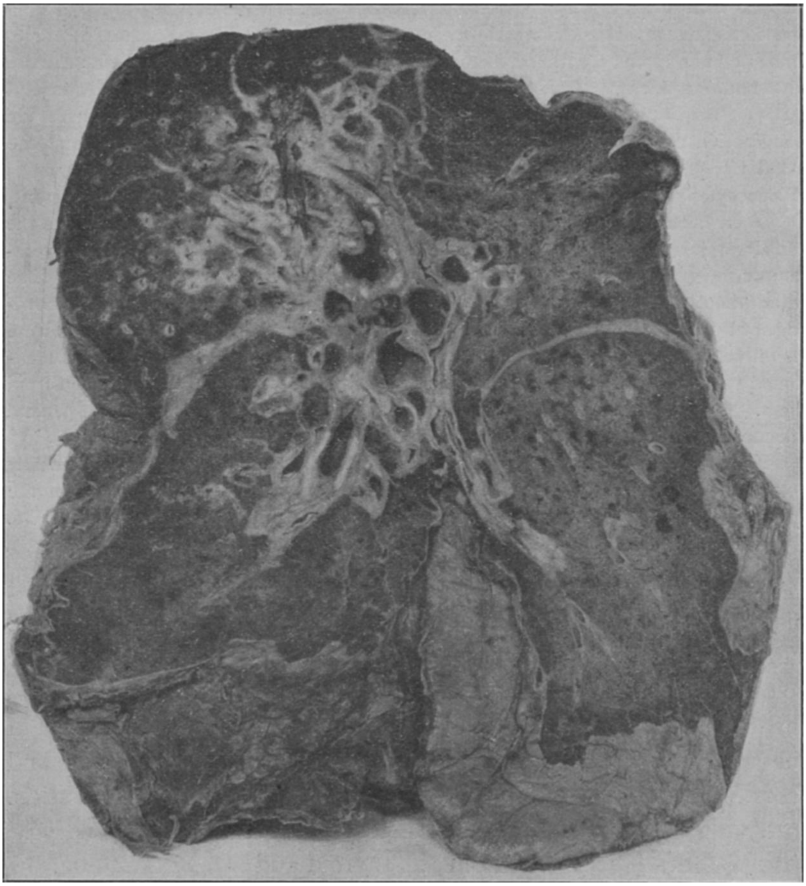

FIG. 1.—The peribronchial fibrous tissue at the root of the right lung, the white zones of infiltration about the smaller bronchi of the upper lobe and the nodules on the diaphragmatic pleura are well shown.

"In the left fifth intercostal space outside the pleura near the angles of the ribs an abscess occurs surrounded by a heavy wall of tissue, the whole as large as a pigeon's egg. In the right pleural cavity are dense adhesions, and between many of them there is a sero-purulent and blood-stained fluid. Separating these adhesions yellowish elevations resembling tubercles are exposed. They vary in size from some just visible, to 2 mm. in diameter; they are very numerous in the pleura over the diaphragm. On and between them are shaggy masses of pink and partially organized fibrin.

"A large amount of fibrous tissue is found on section of the right lung about the vessels and bronchi at the root and in the obliterated interlobar fissures; even near the periphery the bronchi are unusually conspicuous by their thick walls (see Fig. 1). The lining of the large bronchi appears rough; many of medium caliber are plugged with semi-fluid, blood-stained mucus; in the upper lobe the minute bronchi are also closed. The intervening lung tissue shows no changes except marked anthracosis.

"At the root of the right lung there are moderately enlarged lymph glands which show areas resembling caseation; they are otherwise quite black from coal pigment.

"The left lung weighs 300 grams; there are changes similar to those in the right lung in a small region near the apex; the remainder of the lung is emphysematous.

"In removing the lungs and organs of the neck an abscess is exposed posterior to the esophagus and extending upward into the neck from the upper dorsal vertebrae. Its walls are the two plurae laterally and the eroded vertebrae behind; it has extended upward higher than the erosion of the vertebrae. The pus is thick and yellowish. The anterior surface of the second dorsal vertebra is the seat of a shallow erosion occupying the entire surface; the anterior half of the body of the third, the entire body of the fourth, and posterior half of the body of the fifth dorsal vertebrae are absent. There are found only a few fragments of the fourth, mainly the spinous and articular processes, imbedded in edematous granulation tissue of the abscess marking the gibbus. The intervertebral cartilage between the second and third vertebrae projects forward between the adjacent erosions. The cartilages on either side of the fourth are absent. The changes of the plurae on both sides are in direct continuity with the lesions of the vertebrae, and a part of the upper lobe of the right lung remains adherent. A fistulous passage from the right pleural cavity extends into the spinal canal, opening behind the body of the third dorsal vertebra by an irregular hole 1 cm. in diameter.

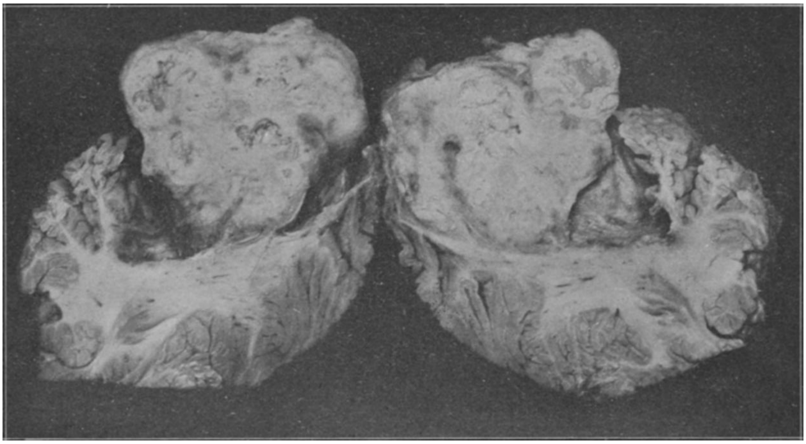

FIG. 2.—The large nodule in the cerebellum apparently made up of a number of coalescent smaller nodules with softening in their centers.

'There is a sheath of firm blastomycotic granulation tissue surrounding the dura opposite the carious vertebrae; this sheath, on the front of the cord, is 5 cm. in length, and here it is 1 cm. higher posteriorly (see Fig. 6). It is very irregular in shape, flattened out in front opposite the destroyed fourth vertebra, and extremely nodular and thick behind at the same point. Cross-section at the greatest diameter shows the width of the tissue outside the dura to be 7 mm. The tissue is made up of easily recognized coalescent nodules, 1 to 2 mm. in diameter, white with darker borders. The spinal fluid below this point is clear.

"Over an area 2.5×1 cm. at the outmost angle of the right lobe of the cerebellum the pia is hyperemic with a pearly white border. This area is smooth, slightly elevated, and the sulci of the cerebellum are absent. A horizontal section here shows that nearly the entire external half of the right lobe of the cerebellum resembles a huge "solitary tubercle" with more liquefaction necrosis than usual in tuberculous brain lesions (see Fig. 2). There are coalescent regions of softening with wide margins of necrotic tissue in which minute nodules, similar to those about the cord, are present. The region so altered measures 4.5 cm. anteroposteriorly and laterally, and 3.8 cm. in its vertical diameter; it extends to within 2 cm. of the median line. The lesion as a whole is deeply seated, only a small portion of its periphery being in contact with the pia; as already described, the process has not extended through the pia. The remaining brain after hardening, and the pons show no gross changes.

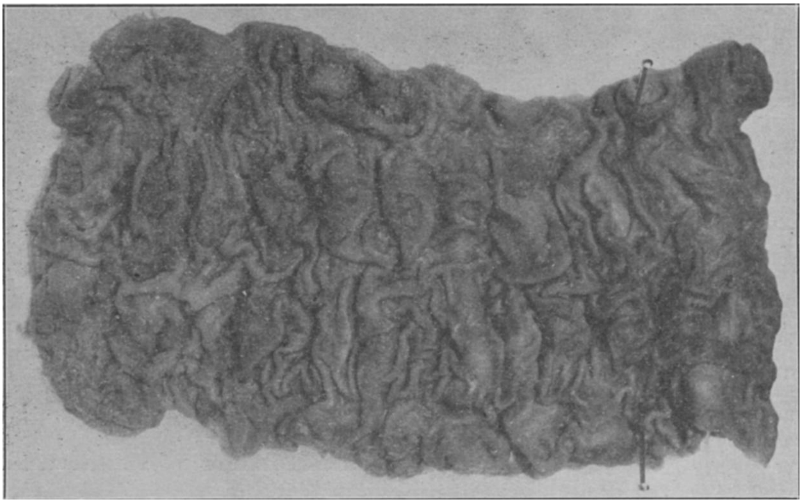

Fig. 3.—The nodules in the colon; careful search failed to reveal blastomycetes.

"The liver weighs 1,900 grams. There are a few minute areas found on the cut surface resembling tubercles. In one kidney similar lesions occur. The spleen weighs 200 grams and is firm.

"There are many pouches externally on the descending colon arranged in rows between the longitudinal bands; these are nipple-shaped and quite symmetrical both in size and arrangement. The lining is found elevated in folds extending between the pouches and around the circumference of the bowel, and on these folds are conicalshaped, round, or slightly oblong nodular swellings (see Fig. 3). This condition prevails for a distance of about 15 cm. in the descending colon; the remaining bowel shows no changes. The nodules vary slightly in size and form, but are otherwise very similar in appearance. The largest are from 1 to 1.5 cm. in diameter, have very high margins and a sharply defined central necrosis. In many the central necrotic portion projects higher than the remainder of the nodule. This necrotic tissue is gray, but its junction with the adjacent tissue is the seat of minute hemorrhages."

The relatives desiring as little mutilation as possible, joints and bones were not further examined, nor were attempts made to cultivate blastomycetes, the nature of the disease having been thoroughly established by the previous observers, Eisendrath and Ormsby.

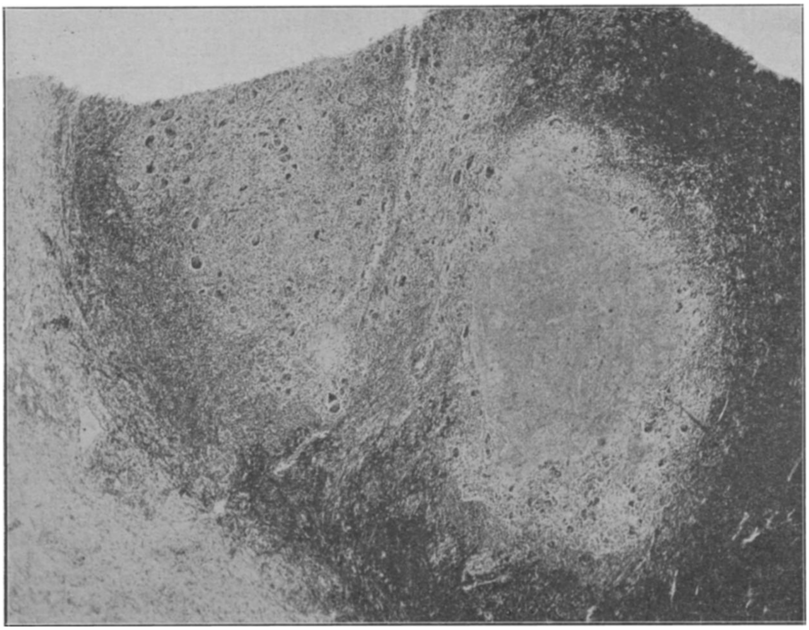

FIG. 4.—Blastomycotic nodules in the bronchial lymph glands. The one to the right shows an eosin-staining necrotic center resembling similar regions in tuberculous lymph glands very closely. (× 25)

Cover-glass preparations of the pus in the cerebellar lesion showed an abundance of blastomycetes, and budding forms were easily found. Cultures from the various viscera resulted in the isolation of the colon bacillus only; consequently there was no generalized mixed or secondary bacterial infection as, for example, was found in the case reported by Irons and Graham.[1]

Histologic examination.—Sections of the affected lung tissue show the changes described by Irons and Graham[2] the process is essentially broncho-pneumonic and more a bronchitis than a pneumonia. In many sections the bronchioles are so obliterated that their location is only evident from the peribronchial deposits of coal dust. The lesions in such places resemble those of tuberculosis very closely. The differences noted by other observers are present; a more highly cellular process, less necrosis, more numerous giant cells with blastomycetes. In adjacent alveoli plasma cells and polymorphonuclear leucocytes are abundant. Farther away from the blastomycotic bronchitis the lung tissue shows evidence of edema with many pigment-carrying cells in the alveoli. The pneumonic process about the large bronchi is peculiar in that the cellular exudate is almost entirely made up of plasma cells. Among these are the short rows of cubical epithelium believed to originate by proliferation and metaplasia from alveolar epithelium and common to all chronic inflammations of lung tissue, In many sections the tissue about these large bronchi has more of the characteristics of granulation tissue, and so-called "miliary abscesses," really submiliary and microscopic, occur scattered through it. The centers of these are necrotic, and giant cells with fungi are abundant where the necrotic, tissue joins the surrounding granulation tissue.

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[1] *Jour. Infect. Dis.*, 1906, 3, p. 666.

[2] *Loc. cit*

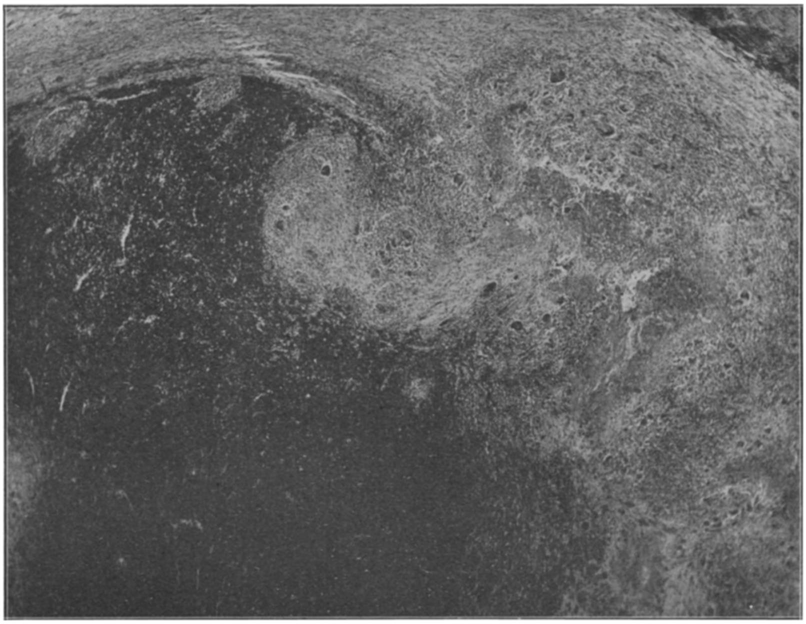

Fig. 5.—Showing the extension outward into the capsule of a bronchial gland. In other places the perilymphadenitis is continuous with the blastomycotic regions in the glands. (× 30)

In the lymph glands about the large bronchi (see Fig. 4) similar blastomycotic nodules occur; the necrotic centers, as a rule, stain with eosin; some show large amount of nuclear débris. Many of the nodules are continuous through the capsule of the gland with the granulation tissue described about the large bronchi and blood vessels, perilymphadenitis (see Fig. 5). Necrosis in these nodules is not marked, and wide zones of incircling fibrillated cells with many multinucleated cells constitute, perhaps, the chief feature.

The giant cells almost invariably contain one or more fungi, and many contain coal pigment as well. Parts of the glands are heavily filled with coal dust. The fungi are often budding and in some instances appear to crowd the giant cells; it is very difficult to find blastomycetes except within the giant cells; even small giant cells contain six or eight fungi. The fungi are readily found with ordinary stains because of their characteristic unstained double-bordered rim and the fine granules that they invariably contain. These granules, which are very minute, vary in size slightly and number four to eight in the single organism; they stain with hematoxylin and with basic anilin dyes.

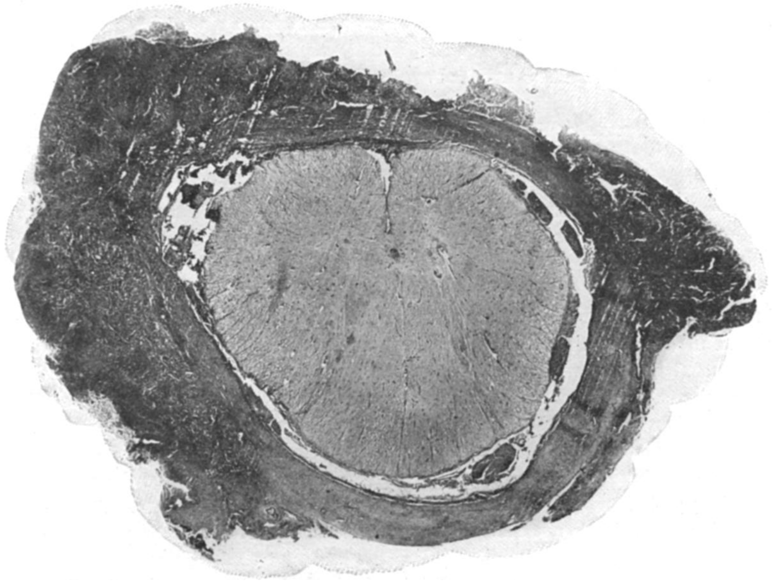

FIG. 6.—The spinal cord and extra dural blastomycotic granulation tissue. The compression and the distortion of the cord is well shown, also the peripheral vacuolation (edema?) in the cord. (× 12$\frac{3}{5}$)

The nodules on the pleura have the usual structure of blastomycotic lesions. The necrosis in some is extensive. The sections of the liver show no blastomycotic lesions; the liver cells contain quite uniformly small granules of a golden-brown color and appear narrow (atrophy). The capillaries are wide and, in the centers of many lobules, sinus-like. In the spleen there is some hyperemia, but in other respects the organ shows no changes. There is no evidence of amyloid infiltration.

In the colon there is less necrosis than the gross appearances indicated, the chief retrogressive change being the disappearance of the glands in oblong regions as wide as two to four of the glands, due to an infiltration with plasma cells and many eosinophilous leucocytes. In the tunica propria about such regions the lymph channels are filled with similar cells. Many of the glands adjacent to these changes are dilated and filled with cells in various degrees of necrosis; they appear like minute cysts, but mucin is not present in any abnormal amounts either in them or in the columnar epithelium. Where these changes occur the mucosa and submucosa project toward the lumen of the bowel, and in the latter coat the veins are greatly dilated. The gross appearance of nodular elevations in the bowel no less than the character of the cellular exudate led to the expectation that fungi would be found; although careful search was made in many sections from various places, the results were entirely disappointing; not only were fungi absent, but both giant cells and abscesses as well.

The changes in the kidney, except for minute blastomycotic focal lesions, are not marked. The secretory epithelium is low, and the convoluted tubules have wide channels. There is considerable hyperemia. The blastomycotic lesions are not numerous; many sections show none and some are partially cicatrized without fungi; others possess both giant cells and fungi.

Sections of the stomach, small intestine, adrenals, mesenteric lymph glands, prostate, and testicles show no noteworthy alterations. The changes in the subcutaneous tissues from the region of the gibbus possess one interesting feature. The necrosis is like that in the lymph glands at the root of the lung. In the latter situation the similarity with the necrosis of tuberculosis (see Fig. 4) led to a careful search for tubercle bacilli on the supposition that latent tuberculosis in the glands might be present as well as blastomycosis; no bacilli were found. In other respects the subcutaneous blastomycosis answers to the descriptions repeatedly given in the literature of this subject.

Sections studied from all portions of a thin slice through the largest diameters of the cerebellar lesion show regions of necrosis separated by well-stained tissue. The necrotic tissue, more frequently reacting to hematoxylin than in the lymph glands and lungs, usually forms small areas, but some are 4 to 7 mm. in diameter. Even in the larger eosin-stained necrotic areas the structure can be made out, and it is evident that necrosis was preceded by the changes present in the enveloping bands and partitions of granulation and inflammatory cerebellar tissue. This meshed arrangement is not uniformly definite in the various sections examined, in places the margins are as distinct as is usually the case in either gumma or solitary tubercle. At numerous points, however, this is not the case; two conspicuous features of the process serve to interrupt the sharpness of the margins.

One is the occurrence in the partitions of minute foci corresponding in all respects to the early changes termed "abscesses." Many of these are so minute as to be readily contained in the field of the oil-immersion lens, or even a small portion of it. The smallest consist of a few spaces the size of those in the fat cells; there is some reason to believe these abscesses contained fluid in the fresh condition, probably serum or a few cells resembling lymphocytes. Fungi occur in the most minute abscesses either in the centers or in the peripheries, more often the latter, where they occupy giant-cells which resemble irregular aggregations of cells much more than giant cells of the Langerhans type. In the larger foci of this kind the fungi are invariably in and among the giant-cells which beset the circumference at many points. The abscesses are so abundant in the tissue about the regions of necrosis that the partitions between them in many places appear honey-combed (low powers). The cells in the abscesses are mono- and polymorphonuclear leucocytes, rarely with evidence of nuclear fragmentation or other signs of necrosis, except near the margins of the large regions of necrosis first mentioned.

The other feature of this cerebellar lesion, and one which also constitutes a difference between it and the nodular lesions of both syphilis and tuberculosis of the central nervous system, is the presence in the well-stained partitions, or the tissue incircling the regions of necrosis, of masses of granulation tissue (see Fig. 7). Such masses are not nearly so common as the abscesses described. They are very cellular; approximately one-half are cells with spindle-shaped, faintly stained nuclei, and cells with small round nuclei, apparently of the fixed tissues; the other half is made up of plasma cells, small mononuclear leucocytes, giant-cells, and a few polymorphonuclear leucocytes. There is no order of arrangement in this granulation tissue as in the tissue about the abscesses, nor have the regions any similarity as regards size. Some seem to be formed by the collapse or compression of abscesses. Other larger masses occur in which apparently abscess formation failed to take place or some degree of healing occurred. It is in these larger masses that aggregations of fungi are found remarkable in their great number, the minute size of the organisms, and the absence of budding (see Fig. 8). Budding forms are quite generally met with in blastomycotic tissues; most authors have described them, and in this case they are readily found among the larger organisms in other regions of blastomycosis as well as in that in the cerebellum; but among these clusters of minute forms in this granulation tissue budding is not present to a degree which would account for, or be in conformity with, their grouping in clusters or their number or small size, which last feature, it is believed, indicates

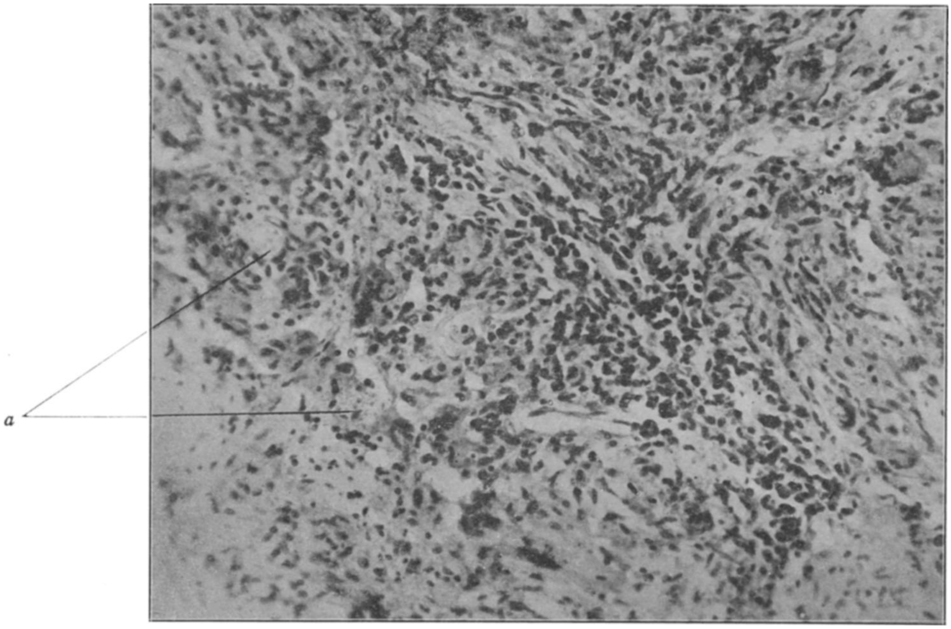

FIG. 7.—The region of blastomycotic tissue in the cerebellum in which the aggregations of young organisms were found and the appearances of sporulation. (*a*) Clusters of fungi. (× 225)

that they are young and newly produced. The hematoxylin-staining granules which the organisms contain do not vary much in size whether the organism is large or small. Many of the blastomycetes in these aggregations are so minute that they are but little larger than the dark granules they contain (see Fig. 7), and the granules are comparable in size with the nucleoli of cells or the granules of chromatin within the nuclei of the plasma cells. With these ideas in mind, search for some other method of reproduction than budding finally resulted in finding large empty organisms, and some of them ruptured, resembling shells or capsules among the clusters of minute young forms. The rounded ends of the membrane at the points of discontinuity are so distinct in some of these (see Fig. 9) that it is difficult to explain the rupture as an artefact.

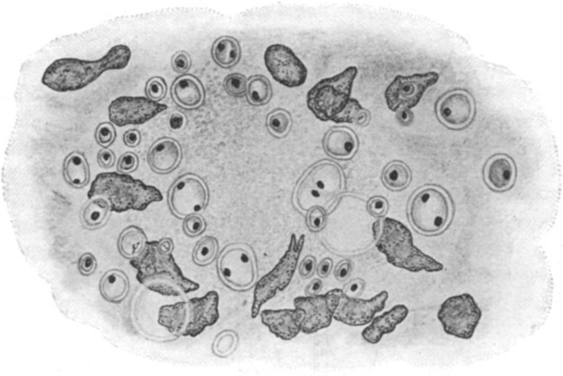

Fig. 8.—Showing the great number of minute fungi and the absence of budding forms among them, in and about a "giant-cell."

The idea that sporulation or another method of reproduction than budding has occurred in the cerebellar lesion has still other arguments in its favor, in that the larger organisms contain a number of the dark granules, the minute forms but one, and the intermediate forms are proportionately provided with them (see Fig. 8). Around the granules there is usually a pale unstained region (see Fig. 10), but this does not appear until the organisms have attained some size.

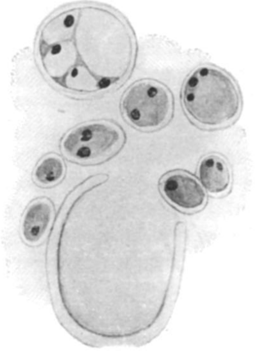

Fig. 9.—Several such empty, large organisms were found with many small forms about them; the rounded ends of the breaks in the membrane of the one represented here were especially distinct.

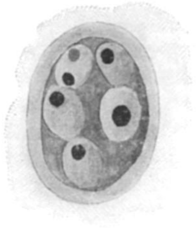

Fig. 10.—The dark granules react to hematoxylin; rarely are more than 8 found in an organism each surrounded with clear zones. The intervening material reacts slightly to hematoxylin.

The extradural sheath of blastomycotic tissue about the spinal cord shows no features of special interest. It is highly vascular, and necrosis is not marked. In places minute foci—"blastomycotic tubercles or abscesses"—occur, but for the most part they are so massed together that their identity is lost or recognized with difficulty. Giant-cells, mainly with peripheral nuclei, are abundant, and the fungi are no more numerous than is usual in blastomycotic granulation tissue; no such clusters of minute forms as in the cerebellum can be found; as a rule, the giant-cells contain organisms, a few occur free among the cells.

Where the cord has suffered compression (see Fig. 6) and distortion there are found in its peripheral portions many minute holes (edema ?) forming a zone in many sections one-tenth the diameter of the cord; in other sections the entire white substance shows these changes. In numerous places the holes are so large that the peripheral parts of the cord are reduced to a network. In sections stained with the Weigert-Pal method there are degenerative changes in the posterior median columns above the region of compression and marked in the cervical enlargement; at this level there are also similar changes in the direct cerebellar tracks. Opposite the external pachymeningitis marked, almost complete, degeneration was found of one of the posterior roots. Below, there are changes in the pyramidal tracts, more marked in the lumbar enlargement than in the lower dorsal region. These changes are not complete degeneration in any of these locations, except perhaps the posterior nerve root mentioned; they are less marked below than above the point of invasion of the spinal canal; in all places some well-stained myelin sheaths are found when the higher powers of the microscope are used.

One notable feature of this case is the large conglomerate blastomycotic nodule in the cerebellum. In only one other case of systemic blastomycosis, that of Curtis,[1] is there any record of changes in the nervous system, and the statements in that instance are solely clinical, that death was due to meningitis. The reproduction by a process of sporulation demonstrable in the cerebellar lesion is likewise a new feature of the changes encountered in the lesions of this disease. The idea that in the nervous tissues the fungus may have found favorable or different conditions of nutrition, as an explanation for this method of multiplication, is opposed by the facts that the regions in which it was found were very minute, that it was not generally present in the cerebellar process, and that budding was commonly observed in the "abscesses" in the partitions between necrotic regions.

Highly interesting is the relationship between this case of blastomycosis and the coccidioidal disease described by Ophüls.[2] Up to the present two of the chief differences between blastomycosis and coccidioidal granuloma have been the endosporulation observed in the tissues in the latter disease and its tendency to spread by the lymph channels. Although no widespread extension by the lymphatics was demonstrated in the case reported here, the extension to the tracheo-bronchial glands and in peribronchial lymph channels is unmistakable; the endosporulation in the cerebellum in part also resembles the methods of reproduction described for the organism of coccidioidal granuloma. Taken together, these features in this instance of systemic blastomycosis are in accord with the belief expressed by Ophüls[1] of a close relationship of the organisms in the two diseases.

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[1] *Ann. de l'Inst. Pasteur*, 1896, 10, p. 448.

[2] *Jour. Exp. Med.*, 1901–5, 6, p. 443; also *Jour. Am. Med. Assoc.*, 1905, 45, p. 1291.

The failure to find blastomycetes in the nodules in the colon has in no degree impaired our belief in their blastomycotic nature; the gross and minute characteristics of the changes there are so different from any form of ulcerative colitis with which we are familiar, and so much in accord with the lesions of blastomycosis generally, that without the clinical observation of the fungi in the feces it would still seem highly probable that the lesions represent a blastomycotic colitis.

Finally it is apparent that in the growing literature on systemic blastomycosis, new forms of disease, at least anatomically, are constantly being added to those previously recorded. Numerous summaries of the literature have been made; they are of great value in the recognition of new cases; it must be remembered, however, that as yet the carefully studied examples of this disease are few,[2] and that in future observations still other manifestations may be encountered.

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[1] *Jour. Exp. Med.*, 1901–5, 6, p. 443.

[2] This is the seventh report of postmortem examination of systemic blastomycosis.